A thesis of the Master's degree

Association between Sleep Quality and Metabolic Syndrome in Korea

수면의 질과 대사증후군과의 관련성

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Abstract

Introduction: To determine whether a simple, structured self-report of overall sleep quality is associated with the presence of the metabolic syndrome and its components.

Methods: An observational, cross-sectional study comparing global score on the Pittsburgh Sleep Quality Index (PSQI) with concurrently collected measures of the components of the metabolic syndrome and presence or absence of the syndrome. A total of 3,057 adults, aged 18 - 80, who visited the Center for Health Promotion of Seoul National University Hospital in Korea between January 2010 and December 2011, were included in this study. The sample included 2,076 males (67.9%) and 981 females (32.1%). The prevalence of metabolic syndrome in our sample was 21.5% (27.0% for males and 10.0% for females). The subjects were divided into two groups of poor sleeper group (n = 529) vs. good sleeper group (n = 2,528) by the Pittsburgh Sleep Quality Index global score. The components of metabolic syndrome, serum levels of insulin and abdominal computed tomography (CT) scans were measured. The metabolic syndrome criterion of the AHA/NHLBI 2005 was adopted. All analyses were adjusted for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs.

Results: Logistic regression results showed that global sleep-quality score on the PSQI were not related significantly to the presence of the metabolic syndrome (OR = 1.07, 95% CI: 0.79 - 1.44 for males; OR = 1.16, 95% CI: 0.66 – 2.02 for females). The multiple-regression results showed that the PSQI global sleep-quality score was not related to abdominal visceral fat, insulin levels, insulin resistance and most metabolic syndrome components significantly. However, poor sleep quality was related to high-density lipoprotein ($p = 0.014$) positively among males, and the predictor of waist circumference ($p < 0.001$) and body mass index ($p = 0.009$) gain among females.

Conclusions: In conclusion, self-reported global sleep quality is not related to metabolic syndrome and most its risk factor components. However, obesity is associated with poor sleep quality in women. Additional prospective cohort

studies are needed to evaluate relationships among these measures, the behavioral and physiologic mechanisms that link sleep quality and metabolic disorders.

Keywords: Metabolic syndrome, sleep quality, abdominal visceral fat, insulin resistance, Pittsburgh Sleep Quality Index

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Introduction

Metabolic syndrome represents a cluster of coronary heart disease risk factors, including obesity (particularly abdominal adipose tissue), elevated blood pressure, high fasting plasma glucose and triglyceride concentrations, and low serum high-density lipoprotein cholesterol levels (1). The importance of central obesity and abdominal fat mass has been known to have a stronger relation to the prevalence of each component of metabolic syndrome (hyperglycemia, diabetes and hypertension) than body mass index (BMI) (2). Increased insulin levels and insulin resistance are defined by some as part of the metabolic syndrome but are considered by others as an underlying cause for the syndrome (3-6). When initially identified, the clustering of these risk factors was thought to be induced by dysregulation of insulin (3). However, the pathophysiologic basis of the metabolic syndrome remains in doubt (7,8). Indeed, some have questioned the clinical value of identifying the syndrome despite the associations between the syndrome and disease incidence (6).

Chronic sleep debt, which is increasingly common in developed countries, is associated with metabolic and endocrine alterations that may have pathological consequences in the long term (9,10). Regarding sleep duration, both short and long are associated with metabolic syndrome (11-13). In addition to sleep duration, Jennings et al. showed that the low sleep quality is associated with metabolic syndrome in a sample of two hundred and ten Caucasian adults (14). A Taiwanese study has showed that subjects who have higher global PSQI score and a higher risk of being poor sleepers are more likely to relate to metabolic syndrome (15). Reduced sleep quality without changes in duration is associated with insulin resistance (16,17) and sleep disturbances are also related to diabetes (18) and all-cause mortality (19). Despite these associations, not all studies have found sleep disruption and metabolic disease to be related. For example, one recent report failed to find a relationship between sleep disturbance in midlife in women and subsequent incidence of diabetes (20). In the Coronary Artery Risk Development in Young Adults Sleep Study, both

shorter sleep duration and greater sleep fragmentation were not with markers of glucose metabolism in non-diabetic middle-aged adults (21).

The Pittsburgh Sleep Quality Index (PSQI) is a widely used and well-validated measure of sleep quality, and is suitable for epidemiologic investigations (22,23). There are limited studies that explore whether the PSQI sleep quality is related to computed tomography (CT) abdominal fat, insulin resistance and metabolic syndrome in a large sample study. The objective of this study was therefore to examine the relationship between sleep quality and metabolic syndrome in 3,057 Korean people, who were examined with CT scanning of the abdomen and measured with fasting blood samples of insulin, which are valid biomarkers to understand the mechanism of metabolic disorders, using the PSQI.

Materials and Methods

1. Subjects

From January 2010 to December 2011, 10,727 subjects visited the Center for Health Promotion of Seoul National University Hospital for a routine health check-up. Exclusion criteria included clinical history of coronary artery disease, cerebrovascular diseases, cancer diagnosis or treatment within the past year, chronic liver or kidney disease, thyroid disease, pregnancy and weight-loss. The subjects, younger than 18 years or older than 80 years were also excluded. Of 3,682 participants who completed the PSQI and were identified the above exclusion criteria, 622 subjects were excluded because of not completing a structured questionnaire, which included marriage, education, job, income, smoking history, alcohol use, stress, anxiety, depression and physical activity. Three subjects, who had extreme data on high-density lipoprotein cholesterol (HDL-C) and diastolic blood pressure (DBP), or was missing of blood samples information, were excluded. Finally, this left data from 3,057 participants, aged 18 to 80. The institutional review board of Seoul National University Hospital approved the study.

2. Sleep-Quality Assessment

The PSQI has been widely used and has good psychometric properties. The instrument, its reliability, and its validity are presented in Buysse et al (22). Nineteen items generate a global sleep-quality score, as well as score on 7 components of sleep quality: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. A higher global PSQI score indicates poorer sleep quality, and a global PSQI score greater than 8.5 has a diagnostic sensitivity of 94.3% and specificity of 84.4% in differentiating poor from good sleepers. The Korean version of the Pittsburgh Sleep Quality Index has an

overall reliability coefficient of 0.84, and acceptable test-retest reliability with a coefficient of 0.65 (23).

3. Risk-Factor Assessments

All subjects underwent physical examinations by trained personnel who used a written, systematic protocol with standardized instruments. Wearing light indoor clothes, each subject's body height (to the nearest 0.1 cm), weight (to the nearest 0.1 kg), and waist circumference (to the nearest 0.1 cm) was measured. Waist circumference measurement was performed at the end of normal expiration in duplicate on bare skin midway between the lower rib margin and the iliac crest. BMI was calculated as weight (in kilograms) divided by height (in meters) squared. For blood pressure measurement, each subject rested 10 minutes in a supine position in a quiet ambience, and two measurements were obtained with an automated machine between 7:30 AM and 11:00 AM. All subjects underwent 12-h overnight fasting and blood sampling for basic biochemical examinations, such as triglyceride, HDL-C, fasting blood sugar (FBS) and so on.

Serum triglyceride, HDL-C, FBS and insulin were determined in the laboratory of Seoul National University Hospital. Insulin resistance was estimated from the homeostasis model assessment (HOMA-IR) = serum insulin (μIU/mL) × fasting blood glucose (mmol/L)/22.5 (24).

Subjects were examined with a 16 detector row Somatom® Sensation 16 CT scanner. CT was done between the fourth and fifth lumbar vertebrae. The cross-sectional surface areas of the abdominal fat compartments (visceral adipose tissue and total adipose tissue) were calculated using Rapidia 2.8 CT software (Infinitt, Seoul, Korea) with attenuation ranging from -250 to -50 HI to separate fat tissue. Subcutaneous adipose tissue (SAT) area was obtained by subtracting visceral adipose tissue (VAT) from total adipose tissue.

Metabolic syndrome was defined according to National Cholesterol Education Program (NCEP) criteria as the presence of three or more of the following five criteria (1).

[1] A waist circumference greater than 90 cm in males or greater than 80 cm in females;
[2] A fasting serum glucose level of 100 mg/dL or higher or the use of diabetes medication;
[3] A blood pressure of 130 mmHg systolic/85 mmHg diastolic or higher or the use of antihypertensive medication;
[4] A serum triglyceride level of 150 mg/dL or higher or the use of medication for dyslipidemia
[5] A high-density lipoprotein (HDL) cholesterol level of less than 40 mg/dL in males or 50 mg/dL in females or the use of medication for low HDL cholesterol.

4. Confounders

At the time of health check-up, all subjects completed a self-administered questionnaire, which included questions about education, smoking history, alcohol use, stress, anxiety, depression, physical activity, menopause (female) and so on. Education was grouped into 3 categories, "less than high school," "high school graduate," and "more than high school." Smoking history was categorized as nonsmoker, past smoker, and current smoker. For alcohol use, participants were asked if they were nondrinkers, past drinkers and current drinkers. BEPSI refers to Brief Encounter Psychosocial Instrument. Anxiety and depression were measured by Goldberg's short screening scale for anxiety and depression (25). Physical activity measured by the short last-seven-day self-administered format of the International Physical Activity Questionnaire (IPAQ) , which was grouped in to low, moderate and high (26). Snoring is defined as coughing or snoring loudly three times or more a week during the past month. Menopausal status was recorded as premenopausal, menopausal transition and menopausal.

5. Analysis

Our hypothesis is that the prevalence of metabolic syndrome among poor sleepers group is higher than good sleepers group.

Null hypothesis is that the prevalence of metabolic syndrome among poor sleepers group and good sleepers group is equal.

Alternative hypothesis is that the prevalence of metabolic syndrome among poor sleepers group and good sleepers group is unequal.

According to prior data, if the prevalence of metabolic syndrome among good sleepers group is 0.22, the prevalence of metabolic syndrome among poor sleepers group is 0.30, and power is 0.8, we will need to study 962 subjects, which were enough to conduct an experiment for us using the stratified analysis by gender (15).

According to the univariate analysis of sleep quality and metabolic syndrome, we select age, snoring, use of hypertensive drugs as confounders, which were statistical significant ($P < 0.05$). After controlling for menopausal status, the results were unchanged. In addition, for the limitation to include at least 962 subjects to study, we did not select menopausal status as confounder, which has much missing data. Regarding to marriage status, job, income, which were partly associated with poor sleep quality and metabolic syndrome in the present study, we just take out them to analysis the baseline characteristics of subjects more clearly and deeply, for the reason that there were nearly no effects in the process of statistical model building. Because education, alcohol use, smoking history, stress, anxiety, depression, physical activity are associated with sleep quality and metabolic syndrome in the preceding studies (27 – 32), which showed statistical significant ($P < 0.05$) in parts of our study results, we also take them account into as confounders. More importantly, after controlling for these confounders, the statistical model became more reliant.

The statistical model:

$$Y= a_0 + a_1X_{ag} + a_2Xed + a_3X_{al} + a_4X_{sm} + a_5X_{st} + a_6X_{ax} + a_7X_{dr} + a_8X_{pi} + a_9X_{sn} + a_{10}X_{uh}$$

ag = age, ed = education, al = alcohol, sm = smoking, st = stress, ax = anxiety, dr = depression, pi = physical activity, sn = snoring, uh = use of hypertensive drugs.

Because triglycerides, FBS, HDL, insulin and HOMA data were skewed, the square root of a negative reciprocal, a negative reciprocal and logarithmic transformations were conducted separately.

We compared sleep quality and metabolic syndrome categories using t-test or chi-square test. The results are expressed as the mean (SD) or frequency (%). All statistical analyses were conducted separately for each gender. Continuous variables, including VAT, SAT, HOMA, Insulin were divided into subgroups. A logistic-regression analysis was performed using STATA software (version 11.2; STATA Corp, Houston, TX) with presence or absence of the metabolic syndrome as the dependent variable and the PSQI global sleep-quality score as the predictor variable, controlling for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs. The same predictor was then used in a multiple-regression relating PSQI to VAT, SAT, HOMA (24) and each of the metabolic-syndrome component risk factors.

Results

In this study, 17% of the current sample scored in the poor-sleeper range (global sleep-quality index > 8.5). Blood pressure and serum indexes were reasonably typical for healthy individuals in this age range. 21.5% of the participants met the criterion for the metabolic syndrome.

Among males, poor sleep quality was related to marriage status ($p < 0.001$), alcohol use ($p = 0.044$), stress ($p < 0.001$), anxiety ($p < 0.001$), depression ($p < 0.001$), and snoring ($p < 0.001$) positively in statistical significant. However, sleep quality is poorer in younger subjects among males ($p = 0.001$). In addition, job ($p = 0.022$) was also associated with sleep quality among males (Table 1A).

Table 1A. Baseline characteristics of the subjects among males (n = 2,076).

	Good sleeper global PSQI ≤ 5 (n = 1,771)	**Poor sleeper global PSQI > 5 (n = 305)**	P-value*
Age (y)	51.92 ± 11.75	49.53 ± 12.66	0.001
Marriage status			< 0.001
Yes	1,608 (86.4)	254 (13.6)	
No	163 (76.2)	51 (23.8)	
Education			0.700
< High School	138 (87.3)	20 (12.7)	
High School Graduate	378 (85.7)	63 (14.3)	
> High School	1,255 (85.0)	222 (15.0)	
Job†			0.022
Group 1	537 (87.2)	79 (12.8)	
Group 2	409 (87.2)	60 (12.8)	
Group 3	467 (85.4)	80 (14.6)	
Group 4	199 (81.9)	44 (18.1)	
Group 5	159 (79.1)	42 (20.9)	
Income‡			0.890
Group 1	516 (85.6)	87 (14.4)	
Group 2	731 (85.8)	121 (14.2)	
Group 3	466 (84.9)	83 (15.1)	
Alcohol use			0.044
None	255 (89.2)	31 (10.8)	
Past	129 (89.0)	16 (11.0)	
Current	1,387 (84.3)	258 (15.7)	
Smoking			0.109
Non-smoker	395 (87.4)	57 (12.6)	
Ex-smoker	799 (85.9)	131 (14.1)	
Current-smoker	577 (83.1)	117 (16.9)	
Stress			< 0.001
BEPSI < 1.8	1,302 (91.4)	123 (8.6)	
BEPSI: 1.8 - 2.8	443 (74.3)	153 (25.7)	

BEPSI ≥ 2.8	26 (47.3)	29 (52.7)	
Anxiety			< 0.001
GAS score < 3	1,064 (95.4)	51 (4.6)	
GAS score ≥ 3	707 (73.6)	254 (26.4)	
Depression			< 0.001
GDS score < 2	731 (97.1)	22 (2.9)	
GDS score ≥ 2	1,040 (78.6)	283 (21.4)	
Physical Activity			0.211
Low	200 (82.0)	44 (18.0)	
Moderate	638 (85.0)	113 (15.0)	
High	933 (86.3)	148 (13.7)	
Snoring			0.029
< 3 times/week	1,426 (86.2)	229 (13.8)	
≥ 3 times/week	345 (82.0)	76 (18.0)	
Antihypertensives			0.481
Yes	374 (86.4)	59 (13.6)	
No	1,397 (85.0)	246 (15.0)	

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%).

† Sub-category of job: Group 1 (professional/office job) / Group 2 (service/sales job) / Group 3 (agriculture/fishing/blue collar job) / Group 4 (housewife/no job) / Group 5 (etc.) Sub-category of job; ‡ Sub-category of income: Group 1 (<400 KRW / month) / Group 2 (400 - 600 KRW / month) / Group 3 (600 - 800 KRW / month) / Group 4 (≥ 800 KRW / month).

BEPSI refers to Brief Encounter Psychosocial Instrument, GAS refers to Goldberg Anxiety Scale, GDS refers to Goldberg Depression Scale, IPAQ refers to the International Physical Activity Questionnaire. Missing data were excluded in each variables.

Among females, low sleep quality was associated with age ($p = 0.007$), education ($p = 0.002$), income ($p = 0.004$), smoking ($p = 0.027$), stress ($p < 0.001$), anxiety ($p < 0.001$), depression ($p < 0.001$), snoring ($p < 0.001$), use of hypertensive drugs ($p < 0.001$) and menopausal status ($p = 0.009$) positively (Table 1B).

Table 1B. Baseline characteristics of the subjects among females (n = 981).

	Good sleeper global PSQI ≤ 5 (n = 757)	**Poor sleeper global PSQI > 5 (n = 224)**	P-value*
Age (y)	48.59 ± 12.81	51.27 ± 13.87	0.007
Marriage status			0.307
Yes	210 (75.0)	70 (25.0)	
No	547 (78.0)	154 (22.0)	
Education			0.002
< High School	107 (69.0)	48 (31.0)	
High School Graduate	211 (73.8)	75 (26.2)	
> High School	439 (81.3)	101 (18.7)	
Job†			0.202
Group 1	116 (80.0)	29 (20.0)	
Group 2	108 (83.7)	21 (16.3)	
Group 3	74 (72.6)	28 (27.4)	
Group 4	419 (76.2)	131 (23.8)	
Group 5	40 (72.7)	15 (27.3)	
Income‡			0.004
Group1	259 (71.0)	106 (29.0)	
Group2	273 (79.8)	69 (20.2)	
Group3	158 (81.4)	36 (18.6)	
Alcohol use			0.196
None	421 (75.9)	134 (24.1)	
Past	56 (72.7)	21 (27.3)	
Current	280 (80.2)	69 (19.8)	
Smoking			0.027
Non-smoker	701 (78.2)	195 (21.8)	
Ex-smoker	31 (68.9)	14 (31.1)	
Current-smoker	25 (62.5)	15 (37.50)	
Stress			< 0.001
BEPSI < 1.8	518 (85.6)	87 (14.4)	
BEPSI: 1.8 - 2.8	212 (68.4)	98 (31.6)	

BEPSI ≥ 2.8	27 (40.9)	39 (59.1)	
Anxiety			< 0.001
GAS score < 3	363 (93.6)	25 (6.4)	
GAS score ≥ 3	394 (66.4)	199 (33.6)	
Depression			< 0.001
GDS score < 2	215 (93.5)	15 (6.5)	
GDS score ≥ 2	542 (72.2)	209 (27.8)	
Physical Activity			0.989
Low	103 (77.4)	30 (22.6)	
Moderate	141 (77.5)	41 (22.5)	
High	513 (77.0)	153 (23.0)	
Snoring			< 0.001
< 3 times/week	681 (79.2)	179 (20.8)	
≥ 3 times/week	76 (62.8)	45 (37.2)	
Antihypertensives			< 0.001
Yes	96 (63.6)	55 (36.4)	
No	661 (79.6)	169 (20.4)	
Menopausal status			0.009
Premenopausal	320 (81.8)	71 (18.2)	
Menopausal transition	62 (83.8)	12 (16.2)	
Menopausal	316 (73.7)	113 (26.3)	

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%).

† Sub-category of job: Group 1 (professional/office job) / Group 2 (service/sales job) / Group 3 (agriculture/fishing/blue collar job) / Group 4 (housewife/no job) / Group 5 (etc.) Sub-category of job; ‡ Sub-category of income: Group 1 (<400 KRW / month) / Group 2 (400 - 600 KRW / month) / Group 3 (600 - 800 KRW / month) / Group 4 (≥ 800 KRW / month).

BEPSI refers to Brief Encounter Psychosocial Instrument, GAS refers to Goldberg Anxiety Scale, GDS refers to Goldberg Depression Scale, IPAQ refers to the International Physical Activity Questionnaire. Missing data were excluded in each variables.

In men, the presence of metabolic syndrome was related to smoking ($p < 0.001$), physical activity ($p = 0.009$), snoring ($p < 0.001$) and use of hypertensive drugs ($p < 0.001$) positively (Table 1C).

Table 1C. Baseline characteristics of the subjects among males (n = 2,076).

	Metabolic syndrome		P-value*
	Yes (n = 560)	No (n = 1,516)	
Age (y)	51.31 ± 12.15	52.26 ± 11.25	0.107
Marriage status			0.209
Yes	50 (23.4)	164 (76.6)	
No	510 (27.4)	1,352 (72.6)	
Education			0.646
< High School	44 (27.9)	114 (72.1)	
High School Graduate	126 (28.6)	315 (71.4)	
> High School	390 (26.4)	1,087 (73.6)	
Job†			0.637
Group 1	160 (26.0)	456 (74.0)	
Group 2	124 (26.4)	345 (73.6)	
Group 3	160 (29.3)	387 (70.7)	
Group 4	60 (24.7)	183 (75.3)	
Group 5	56 (27.9)	145 (72.1)	
Income‡			0.591
Group 1	172 (28.5)	431 (71.5)	
Group 2	223 (26.2)	629 (73.8)	
Group 3	146 (26.6)	403 (73.4)	
Alcohol use			0.270
None	68 (23.8)	218 (76.2)	
Past	35 (24.1)	110 (75.9)	
Current	457 (27.8)	1,188 (72.2)	
Smoking			< 0.001
Non-smoker	91 (20.1)	361 (79.9)	
Ex-smoker	254 (27.3)	676 (72.7)	
Current-smoker	215 (31.0)	479 (69.0)	
Stress			0.164
BEPSI < 1.8	381 (26.7)	1,044 (73.3)	
BEPSI: 1.8 - 2.8	158 (26.5)	438 (73.5)	
BEPSI ≥ 2.8	21 (38.2)	34 (61.8)	

Anxiety			0.243
GAS score < 3	289 (25.9)	826 (74.1)	
GAS score ≥ 3	271 (28.2)	690 (71.8)	
Depression			0.146
GDS score < 2	189 (25.1)	564 (74.9)	
GDS score ≥ 2	371 (28.0)	952 (72.0)	
Physical Activity			0.009
Low	82 (33.6)	162 (66.4)	
Moderate	213 (28.4)	538 (71.6)	
High	265 (24.5)	816 (75.5)	
Snoring			< 0.001
< 3 times/week	400 (24.2)	1,255 (75.8)	
≥ 3 times/week	160 (38.0)	261 (62.0)	
Antihypertensives			< 0.001
Yes	195 (45.0)	238 (55.0)	
No	365 (22.2)	1,278 (77.8)	

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%).

† Sub-category of job: Group 1 (professional/office job) / Group 2 (service/sales job) / Group 3 (agriculture/fishing/blue collar job) / Group 4 (housewife/no job) / Group 5 (etc.) Sub-category of job; ‡ Sub-category of income: Group 1 (<400 KRW / month) / Group 2 (400 - 600 KRW / month) / Group 3 (600 - 800 KRW / month) / Group 4 (≥ 800 KRW / month).

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In women, the presence of metabolic syndrome was associated with age ($p < 0.001$), education ($p < 0.001$), job ($p = 0.008$), income ($p < 0.001$), snoring ($p < 0.001$), use of hypertensive drugs ($p < 0.001$) and menopausal status ($p < 0.001$) positively. However, the presence of metabolic syndrome was related to alcohol use ($p = 0.001$) and depression ($p = 0.023$) negatively among females (Table 1D).

Table 1D. Baseline characteristics of the subjects among females (n = 981).

	Metabolic syndrome		P-value*
	Yes (n = 98)	No (n = 883)	
Age (y)	58.47 ± 1.03	48.17 ± 12.98	< 0.001
Marriage status			0.100
Yes	21 (7.50)	259 (92.50)	
No	77 (11.0)	624 (89.0)	
Education			< 0.001
< High School	32 (20.7)	123 (79.3)	
High School Graduate	34 (11.9)	252 (88.1)	
> High School	32 (5.9)	508 (94.1)	
Job†			0.008
Group 1	6 (4.1)	139 (95.9)	
Group 2	6 (4.6)	123 (95.4)	
Group 3	14 (13.7)	88 (86.3)	
Group 4	66 (12.0)	484 (88.0)	
Group 5	6 (10.9)	49 (89.1)	
Income‡			< 0.001
Group1	55 (15.1)	310 (84.9)	
Group2	29 (8.5)	313 (91.5)	
Group3	9 (4.6)	185 (95.4)	
Alcohol use			0.001
None	72 (13.0)	483 (87.0)	
Past	7 (9.1)	70 (90.9)	
Current	19 (5.4)	330 (94.6)	
Smoking			0.636
Non-smoker	92 (10.3)	804 (89.7)	
Ex-smoker	3 (6.7)	42 (93.3)	
Current-smoker	3 (7.5)	37 (92.5)	
Stress			0.283
BEPSI < 1.8	61 (10.1)	544 (89.9)	
BEPSI: 1.8 - 2.8	27 (8.7)	283 (91.3)	
BEPSI ≥ 2.8	10 (15.2)	56 (84.8)	

Anxiety			0.115
GAS score < 3	46 (11.9)	342 (88.1)	
GAS score ≥ 3	52 (8.8)	541 (91.2)	
Depression			0.023
GDS score < 2	32 (13.9)	198 (86.1)	
GDS score ≥ 2	66 (8.8)	685 (91.2)	
Physical Activity			0.730
Low	12 (9.0)	121 (91.0)	
Moderate	16 (8.8)	166 (91.2)	
High	70 (10.5)	596 (89.5)	
Snoring			< 0.001
< 3 times/week	74 (8.6)	786 (91.4)	
≥ 3 times/week	24 (19.8)	97 (80.2)	
Antihypertensives			< 0.001
Yes	44 (29.1)	107 (70.9)	
No	54 (6.5)	776 (93.5)	
Menopausal status			< 0.001
Premenopausal	13 (3.3)	378 (96.7)	
Menopausal transition	2 (2.7)	72 (97.3)	
Menopausal	65 (15.2)	364 (84.8)	

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%).

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There was no significant difference in clinical characteristics between good sleepers and poor sleepers in men. Subgroup analysis showed that sleep quality was not related to VAT, SAT, Insulin and HOMA significantly among males (Table 2A).

Table 2A. Comparisons of clinical characteristics between good sleepers and poor sleepers among males.

Variables	Good sleepers	Poor sleepers	P-value*
Main group (n = 2,076)			
N	1,771 (85.3)	305 (14.7)	
BMI (kg/m^2)	24.20 ± 2.79	24.26 ± 2.91	0.705
WC (cm)	88.40 ± 7.90	88.64 ± 8.45	0.614
FBS (mg/dL)	94.64 ± 19.21	95.94 ± 20.82	0.283
SBP (mmHg)	127.25 ± 14.11	126.80 ± 13.78	0.610
DBP (mmHg)	77.41 ± 10.35	77.86 ± 10.57	0.486
TG (mg/dL)	132.93 ± 82.03	141.39 ± 97.19	0.106
HDL-C (mg/dL)	50.53 ± 12.06	51.99 ± 12.10	0.052
Metabolic syndrome	470 (26.5)	90 (29.5)	0.280
Subgroup (n = 635)			
N	554 (87.2)	81 (12.8)	
VAT (cm^2)	110.04 ± 24.52	111.71 ± 28.68	0.576
SAT (cm^2)	114.42 ± 21.98	115.96 ± 27.50	0.570
Insulin (μIU/mL)	6.81 ± 3.98	7.35 ± 5.13	0.275
HOMA	1.64 ± 1.06	1.83 ± 1.37	0.150

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%). BMI: body mass index, WC: waist circumference, FBS: fasting blood sugar, SBP: systolic blood pressure, DBP: diastolic blood pressure, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. HOMA refers to homeostasis model assessment, a measure of insulin resistance.

However, body mass index ($p < 0.001$), waist circumference ($p < 0.001$), fasting blood sugar ($p = 0.006$), diastolic blood pressure ($p = 0.036$) and systolic blood pressure ($p = 0.017$) were related to poor sleepers group positively among females. Though there was a trend that poor sleepers group was related to VAT, SAT, Insulin and HOMA positively, the statistical results were not significant. (Table 2B)

Table 2B. Comparisons of clinical characteristics between good sleepers and poor sleepers among females.

Variables	Good sleepers	Poor sleepers	P-value*
Main group (n = 981)			
N	757 (77.2)	224 (22.8)	
BMI (kg/m^2)	22.37 ± 3.30	23.43 ± 3.34	< 0.001
WC (cm)	7 9.13 ± 9.26	83.16 ± 9.71	< 0.001
FBS (mg/dL)	88.73 ± 14.58	91.99 ± 18.43	0.006
SBP (mmHg)	119.59 ± 16.37	122.56 ± 16.26	0.017
DBP (mmHg)	72.18 ± 10.92	73.93 ± 11.20	0.036
TG (mg/dL)	94.32 ± 48.21	100.29 ± 52.32	0.111
HDL-C (mg/dL)	60.82 ± 13.69	59.26 ± 13.80	0.136
Metabolic syndrome	68 (9.0)	30 (13.4)	0.053
Subgroup (n = 209)			
N	150 (71.8)	59 (28.2)	
VAT (cm^2)	89.18 ± 22.88	94.77 ± 22.89	0.113
SAT (cm^2)	131.68 ± 26.58	138.42 ± 23.73	0.091
Insulin (μIU/mL)	5.99 ± 3.25	6.52 ± 4.54	0.347
HOMA	1.36 ± 0.87	1.47 ± 1.16	0.459

*P values were obtained by t-test or chi-square test. Values are mean ± standard deviation or number (%). BMI: body mass index, WC: waist circumference, FBS: fasting blood sugar, SBP: systolic blood pressure, DBP: diastolic blood pressure, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. HOMA refers to homeostasis model assessment, a measure of insulin resistance.

The PSQI global sleep-quality score was not associated significantly with the presence of the metabolic syndrome. Particularly, odds ratio of metabolic syndrome relating to poor sleep quality (OR = 1.07, 95% CI: 0.79 - 1.44 for males; OR = 1.16, 95% CI: 0.66 – 2.02 for females) decreased relatively, after controlling for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs (Table 3).

Table 3. Results of logistic regression relating the metabolic syndrome to the PSQI global sleep quality score.

	Model 1		Model 2		Model 3	
	cOR	95% CI	aOR	95% CI	aOR	95% CI
Male						
Sleep quality	1.16	0.89 - 1.51	1.18	0.90 - 1.54	1.07	0.79 - 1.44
Female						
Sleep quality	1.57	0.99 - 2.48	1.29	0.80 - 2.08	1.16	0.66 - 2.02

cOR = crude OR.

aOR = adjusted OR.

CI = confidence interval.

Model 1, unadjusted.

Model 2, adjusted for age.

Model 3, adjusted for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs.

Poor sleep quality was not associated with most metabolic syndrome component risk factors in men and women. Subgroup analysis showed that global sleep quality was not related significantly to VAT, SAT and insulin resistance. However, poor sleep quality was related to high-density lipoprotein ($p = 0.014$) positively among males, and the predictor of waist circumference ($p < 0.001$) and body mass index ($p = 0.009$) gain among females (Table 4A and Table 4B).

Table 4A. Multiple regression results relating aspects of the metabolic syndrome to the PSQI global sleep quality score among males (n = 2,076).

	PSQI Global Sleep Quality Index			
Variable	β	SE	t	P-value
Main group (n = 2,076)				
WC (cm)	-0.08	0.51	-0.15	0.884
FBS (mg/dL)	< 0.01	< 0.01	1.54	0.124
SBP (mmHg)	-0.29	0.90	-0.32	0.752
DBP (mmHg)	0.41	0.68	0.61	0.542
TG (mg/dL)	< 0.01	< 0.01	0.18	0.858
HDL-C (mg/dL)	0.04	0.01	2.45	0.014
BMI (kg/m^2)	-0.30	0.18	-0.17	0.868
Subgroup (n = 635)				
VAT (cm^2)	0.35	3.14	0.11	0.912
SAT (cm^2)	0.64	2.84	0.23	0.821
HOMA	< 0.01	0.09	0.03	0.979

Adjusted for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs.

WC: waist circumference, FBS: fasting blood sugar, SBP: systolic blood pressure, DBP: diastolic blood pressure, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, BMI: body mass index, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. HOMA refers to homeostasis model assessment, a measure of insulin resistance.

Table 4B. Multiple regression results relating aspects of the metabolic syndrome to the PSQI global sleep quality score among females (n = 981).

	PSQI Global Sleep Quality Index			
Variable	β	SE	t	P-value
Main group (n = 981)				
WC (cm)	2.74	0.69	3.97	< 0.001
FBS (mg/dL)	< 0.01	< 0.01	0.36	0.715
SBP (mmHg)	0.99	1.22	0.81	0.417
DBP (mmHg)	0.52	0.88	0.59	0.558
TG (mg/dL)	> -0.01	< 0.01	-0.87	0.386
HDL-C (mg/dL)	> -0.01	0.02	-0.22	0.828
BMI (kg/m^2)	0.67	0.26	2.61	0.009
Subgroup (n = 209)				
VAT (cm^2)	3.07	3.53	0.87	0.387
SAT (cm^2)	3.94	4.30	0.92	0.360
HOMA	-0.05	0.12	-0.42	0.677

Adjusted for age, education, alcohol, smoking, stress, anxiety, depression, physical activity, snoring and use of hypertensive drugs.

WC: waist circumference, FBS: fasting blood sugar, SBP: systolic blood pressure, DBP: diastolic blood pressure, TG: triglyceride, HDL-C: high density lipoprotein cholesterol, BMI: body mass index, VAT: visceral adipose tissue, SAT: subcutaneous adipose tissue. HOMA refers to homeostasis model assessment, a measure of insulin resistance.

Discussion

In our analyses of data from aged from 30-81, generally healthy adults, the global sleep quality score, as measured by the PSQI, was not related significantly to the metabolic syndrome. However, J. Richard showed that an increase in the global PSQI score of 2.6 points is associated with a 44% risk of having metabolic syndrome after adjusting for age and gender in Caucasian adults (14). Although J. Richard found positive relationships between global PSQI score and fasting plasma glucose, waist circumference, and BMI, their sample is relatively small. Hung and colleagues show that subjects with metabolic syndrome have a significantly higher global PSQI score, and that the presence of metabolic syndrome is associated with a 0.9 increase in this (15). Their results show that hyperglycemia and low HDL-C were independently associated factors of the global PSQI score, and low HDL-C was the only independent predictor of being a poor sleeper. Unfortunately, they did not consider insulin resistance and abdominal visceral fat which are both vital factors to metabolic syndrome.

The mechanism underlying the association between metabolic syndrome and sleep quality remains unclear. Hypothalamicpituitary-adrenal (HPA) hyperactivity plays a role in the pathogenesis of the metabolic syndrome (33) and activation of the HPA axis can lead to sleeplessness (34). In addition, several short term studies show that sleep fragmentation or restriction lead to insulin resistance (10,12,17,35) which appears to play a key role in the pathophysiology of metabolic syndrome (36). Indeed, chronic sleep debt may have modulatory effects on the glucose metabolism and promote the development of the metabolic syndrome, resulting in sleep disorders which in turn lead to poor sleep quality (37).

This is the first epidemiologic study to investigate the relationship between CT measured abdominal adiposity with self-reported sleep quality in a large sample. Our study is unique in its use of precise measures of abdominal fat areas by CT, fasting blood samples of insulin, metabolic syndrome components which are strongly associated with each other, to explore the relationship of

sleep quality and metabolic disorders using the PSQI. In our study, sleep quality and duration were not appreciably associated with VAT. S Yi' study also found that there is no association between VAT and sleep duration (38). However, in Kim's study, which is cross-sectional, short sleep duration is associated with VAT (39).

We found metabolic syndrome and most of its components were not related to the PSQI global score, which is inconsistent with J. Richard's and Hung's studies (14, 15). However, our study found that poor sleep quality was positively associated with HDL-C in male, and the predictor of waist circumference and BMI gain in female. In Choi's cohort study, the mean HDL levels of participants sleeping less than 6 hours a day were higher than those of participants sleeping 6 to 7.9 and 8 to 9.9 hours a day in men, which was similar with our results (40). Furthermore participants sleeping less than 6 hours had the lowest TG levels compared to the other groups in men. However, Choi and colleagues did only consider sleep duration other than sleep quality in the study, and did not consider mental health such as stress, depression and anxiety. Regarding to increasing waist circumference and BMI among women because of low sleep quality in our research, Cecilia BJ ¨Orkelund's prospective population study gives us a strong support, which found that there is no association between sleep problems and developing diabetes was seen in this 32-year follow-up of middle-aged women. Their results showed that obesity, on the other hand, known to cause increased risk of diabetes, was associated with current sleep problems (20).

The results, that PSQI global sleep-quality score was not significantly associated with VAT and insulin resistance, which are more biologically valid markers of metabolic disorders, may support the result strongly that sleep quality was not related to metabolic syndrome and its component risk factors in our study. In addition, our post-hoc power among males was 0.85 and the power among women was 0.69. However, the post-hoc for all subjects in our study, which of an uncorrected chi-squared statistic was also not significant ($p = 0.475$), was 0.97. The power analysis can support our null hypothesis strongly that the prevalence of metabolic syndrome between good sleepers group and poor sleepers group is equal.

There are several limitations in the present study. First, since this work is cross-sectional in nature, the causal relationship between metabolic disorders and sleep quality score could not be established. Secondly, we did not measure sleep by objective means, such as actigraphy and polysomnography. Furthermore, the PSQI is not related to objective measures of sleep, such as wrist actigraphy and polysomnography, in African Americans (41). Thirdly, we did not exclude the unrecognized confounding variables such as obstructive sleep apnea (OSA) and a few medications (e.g. antipsychotic drugs, glucocorticoids).

In conclusion, self-reported global sleep quality is not significantly related to metabolic syndrome and most its components. However, obesity is associated with poor sleep quality in women. Finally, identification of the proximal behavioral and biologic relationships between sleep and components of the metabolic disorders is essential to conduct prospective cohort studies.

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초록

서론: 수면의 질과 대사증후군과의 관계에 대한 연구는 미미한 실정으로 본 논문에서는 Pittsburgh Sleep Quality Scale (PSQI)을 이용하여 평가한 수면의 질과 대사증후군과의 관계를 알아보고자 하였다.

방법: 단면조사로 수행된 연구로서 수면의 질과 대사증후군지표와의 관계를 알아보자고 하였다. 2010년 1월부터 2011년 12월까지 서울대학교병원 가정의학과 건강증진센터에 내원한 나이가 18-80세의 3,057 명 (남자 2,076명, 여자 981명)을 대상으로 하였다. 이 대상자 중 대사증후군의 유병율은 21.5% (남자 27.0%, 여자 10.0%)였다. PSQI 총점에 따라 불만족스러운 수면군 (n = 529)과 만족스러운 수면군 (n = 2,528), 두 군으로 분류하였으며 수면의 질과 복부비만, 인슐린 저항성, 대사증후군지표와의 관계를 분석하였다. 대사증후군지표 측정, 인슐린 측정, 복부비만 CT (컴퓨터 촬영)을 실행하였다. 대사증후군은 2005년 AHA/NHLBI 에서 제시한 진단기준에 따라 정의하였다. 모든 통계분석은 나이, 교육수준, 음주, 흡연, 스트레스, 불안, 우울, 신체활동, 코골기, 고혈압약물 복용에 대해 보정하였다.

결과: 로지스틱회귀분석에서는 수면의 질과 대사증후군의 관계는 유의한 결과를 보이지 않았다 (남자 OR = 1.07, 95% CI: 0.79 – 1.44; 여자 OR = 1.16, 95% CI: 0.66 – 2.02). 그리고 선형회귀분석에서도 수면의 질과 복부 내장비만, 인슐린, 인슐린 저항성, 대부분 대사증후군 지표들과의 관계는 유의하지 않았다. 다만 남자에서는 불면증과 HDL-콜레스테롤 (p = 0.014)은 양의 상관관계를 보였으나, 여자에서는 불면증과 허리둘레 (p < 0.001) 또는 체질량 지수는 (p = 0.009) 양의 상관관계를 보였다.

결론: 수면의 질과 대사증후군과의 관계는 유의하지 않다. 다만 여자에서는 수면의 질과 비만과의 관련성은 있다. 향후 수면장애 집단

을 대상으로 수면의 질을 향상시키는 중재 프로그램이 대사증후군에 미치는 효과에 관한 전향적인 코호트 연구가 필요할 것으로 여겨진다.

주요어: 대사증후군, 수면의 질, 복부비만, 인슐린 저항성, Pittsburgh sleep quality index

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